DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/24/2011 has been entered.

Applicant's amendment filed on 06/24/2011, amended claims 34, 39, 45, 46, 47, 56, 58, 62, and added new claims 65-73.

Claims 34, 39, 45-47, 56, 58, 62, 65-73 are pending, and examined herein.

35 USC § 103 Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 34, 39, 45, 47, 58, 65-66, 68-70, 72-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Root et al. (Antimicrobial Agents and Chemotherapy. Nov. 1988, pages 1627-1631, PTO-892 of record), in view of Raad et al. (US 6,267,979, PTO1449).

Root et al. teaches a method for disinfecting a catheter by contacting (flushing) with an antimicrobial composition of aqueous EDTA solution having a concentration of 20 mg/ml, 30 mg/ml, 40 mg/ml, 50 mg/ml. The EDTA used by Root et al. is in the form of the disodium salt. Root also teaches that the EDTA is used as a topical antiseptic in gram-negative infections. See page 1627, paragraphs 3, and 6. Root further teaches a sterile polystyrene test tubes (vials) containing the antimicrobial composition of disodium EDTA at a concentration of 20 mg/ml (2 %). See page 1628, lines 18-21; right-hand column, under Experiment 2.

The EDTA used by Root et al. is in the form of the disodium salt. Raad et al., however, teaches that it is known in the art that disodium, trisodium, and tetrasodium EDTA salts have "a significant growth inhibitory effect against species of fungal and bacterial microorganisms including Aspergillus, Fusarium, Candida, Psuedomonas, vancomycin-resistant enterococci, and multidrug resistant Stenotrophomonas". See col.8, lines 26-33; col.9, line 13 to col. 10, line 4; Table 1; and Figures 1-4; column 26, claim 51. EDTA in saline solution is also taught. It would have been obvious to one of ordinary skill in the art to substitute the tetrasodium salt of EDTA for the disodium salt employed by Root et al, as these salts are disclosed to be suitable for use in methods of microbial biofilm disruption. As Root et al discloses using a concentration of 20 mg/ml, the combination with Raad et al. will necessarily have an intrinsic "bactericidal effect over a broad spectrum of microbes and a destructive effect against a variety of yeasts."

It would have been obvious to one of ordinary skill in the art to substitute the trisodium salt of EDTA and tetrasodium salt of EDTA for the disodium salt employed by

Root et al, as these salts are disclosed to be suitable for use in methods of microbial biofilm disruption. As Root et al discloses using a concentration of 20 mg/ml, the combination with Raad et al. will necessarily have an intrinsic "bactericidal effect over a broad spectrum of microbes and a destructive effect against a variety of yeasts."

While the references does not explicitly state that “the lock flush composition has a pH of at least 9.5”, as in claim 65, it is pointed out that as the combined teachings renders the claimed composition obvious, the property of such a claimed composition will also be rendered obvious by the prior art teachings, since the properties, are inseparable from its composition. Therefore, if the prior art teaches the composition or renders the composition obvious, then the properties are also taught or rendered obvious by the prior art. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990.) See MPEP 2112.01.

Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Root et al. (Antimicrobial Agents and Chemotherapy. Nov. 1988, pages 1627-1631, PTO-892), in view of Raad et al. (US 6,267,979, PTO1449) as applied to claims 34, 39, 45, 47, 58, 65-66, 68-70, 72-73 above, and further in view Remington’s Pharmaceutical Sciences.

The combination of references fails to recite the employment of the composition in a prefilled syringe.

Remington’s Pharmaceutical Sciences teaches sterile, pyrogen free solutions of sodium chloride as ideal for injection. It also discloses that hypodermic syringes are

used for injection of liquids. See page 1837. Remington also warns against injection of solutions containing pyrogens (See page 835, column 2, paragraph 1), and to maintain conventional sterile methodology for injected medicaments.

Possessing this teaching by Remington Pharmaceutical Sciences the skilled artisan would have been motivated to provide a syringe filled with an EDTA solution with the expectation of using such sterile, pyrogen free solution for injection.

Claims 62, and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Root et al. (Antimicrobial Agents and Chemotherapy. Nov. 1988, pages 1627-1631, PTO-892 of record), in view of Raad et al. (US 6,267,979, PTO1449) as applied to claims 34, 39, 45, 47, 58, 65-66, 68-70, 72-73, and further in view of Wilder (US 6,500,861, PTO-892 of record).

Root et al., and Raad et al. are applied as discussed above.

Root et al. does not expressly teach that the composition is packaged in a pyrogen free form.

Wider teaches antimicrobial compositions for eliminating infections from various surfaces and materials. It is also taught that the antimicrobial compositions can be administered as a liquid either orally or through a suitable delivery system, such as a catheter. See column 1, lines 8-20; column 2, lines 30-34; and column 4, lines 10-14. It is further taught that the antimicrobial compositions are packaged in a sterile and

pyrogen free form, and can be introduced into the abdominal cavity through a catheter. See column 6, lines 9-10; column 7, lines 51-55.

It would have been obvious to a person of ordinary skill in the art to employ the antimicrobial composition containing tetrasodium EDTA in a sterile pyrogen free condition because Wider teaches antimicrobial compositions as packaged in a sterile and pyrogen free form.

One of ordinary skill in the art at the time of invention would have been motivated to employ the claimed antiseptic compositions in a sterile pyrogen free form as conventional with antimicrobial compositions with the expectation of using the composition in catheters.

Claim 71 is rejected under 35 U.S.C. 103(a) as being unpatentable over Root et al. (Antimicrobial Agents and Chemotherapy. Nov. 1988, pages 1627-1631, PTO-892 of record), in view of Raad et al. (US 6,267,979, PTO1449) as applied to claims 34, 39, 45, 47, 58, 65-66, 68-70, 72-73 above, and further in view of Finch et al. (US 6,679,870, PTO-892).

Root et al., Raad et al., are applied as discussed above.

Root et al., and Raad et al. do not teach ethanol in the EDTA compositions therein.

Finch et al. teaches compositions for disinfecting and locking catheters. The compositions therein contain lower alcohol such as ethanol, isopropanol, and additive

such as EDTA. See abstract. Finch et al. teach that lower alcohol have the ability to inhibit infections. See column 3, lines 20-22.

It would have been obvious to a person of ordinary skill in the art at the time of invention to employ ethanol in the EDTA compositions because Finch et al. teach that the compositions for disinfecting and locking catheters contain ethanol. Accordingly, one of ordinary skill in the art at the time of invention would have been motivated to employ ethanol in the compositions taught by Root et al. with the expectation of success of obtaining compositions for disinfecting catheters.

Claim 56 is rejected under 35 U.S.C. 103(a) as being unpatentable over Root et al. (Antimicrobial Agents and Chemotherapy. Nov. 1988, pages 1627-1631, PTO-892), in view of Raad et al. (US 6,267,979, PTO1449), in view of Wilder (US 6,500,861, PTO-892) as applied to claims 34, 39, 45, 47, 58, 65-66, 67, 68-70, 72-73 above, and further in view of Finch et al. (US 6,679,870, PTO-892).

Root et al., Raad et al., Wilder are applied as discussed above.

Root et al., and Raad et al. do not teach ethanol in the EDTA compositions therein.

Finch et al. teaches compositions for disinfecting and locking catheters. The compositions therein contain lower alcohol such as ethanol, isopropanol, and additive such as EDTA. See abstract. Finch et al. teach that lower alcohol have the ability to inhibit infections. See column 3, lines 20-22.

It would have been obvious to a person of ordinary skill in the art at the time of invention to employ ethanol in the EDTA compositions because Finch et al. teach that the compositions for disinfecting and locking catheters contain ethanol. Accordingly, one of ordinary skill in the art at the time of invention would have been motivated to employ ethanol in the compositions taught by Root et al. with the expectation of success of obtaining compositions for disinfecting catheters.

Claims 65-66, 69, 72-73 rejected under 35 U.S.C. 103(a) as being unpatentable over Hampshire Chemical Corp. (Material Safety Data, 4-5-1993, PTO-892).

Hampshire Chemical Corp. teaches compositions comprising tetrasodium-EDTA in water. The compositions therein are useful as chelating agents.

Hampshire Chemical Corp. does not teach the particular concentration of tetrasodium-EDTA.

It would have been obvious to a person of ordinary skill in the art at the time of invention to determine or optimize parameters such as effective amounts of tetrasodium-EDTA employed in the composition, to obtain a chelating composition. One having ordinary skill in the art at the time the invention was made would have been motivated to determine the effective amounts of tetrasodium-EDTA employed in the compositions, since the optimization of effective amounts of known agents, is considered well in the competence level of an ordinary skilled artisan in science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

35 USC § 103 Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 34, 39, 45, 56, 58, 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fahim (WO 00/13656), in view of Wilder (US 6,500,861, PTO-892).

Fahim discloses antimicrobial compositions comprising about 0.025 to about 8.0 % by weight EDTA or its sodium salts such as tetra sodium EDTA, and the composition has a pH from about 5.0 to about 11.0. See page 10, lines 10-25; and page 11, lines 6-10. It is also taught that the viscosity of the composition can be adjusted by adding sodium chloride. See page lines 15-16. The antimicrobial properties of the compositions were also reported. It is further taught that by increasing the EDTA-Na4 concentration from 2 to 3.0 % by weight provided a substantial increase in bacteria reduction. See page 23, Table 8, prototype 10, wherein the composition comprises 3 % by weight of tetra sodium EDTA, NaCl, water and a pH of 9.5. The antimicrobial compositions comprising tetra-sodium EDTA taught by Fahim are used for topical application such as

for cleaning skin. See page 41, claims 35-37. Regarding, the recitation wherein the solution further comprises 0.5 % to 10 % (V/V) ethanol, the antimicrobial compositions taught by Fahim comprise ethanol. See page 16, lines 3-6, Table 1, Table 2, table 8, wherein it is taught that 8 weight percent of sulfotex, sodium lauryl ether sulfate employed in the compositions therein contains about 13-16 % of ethanol i.e less than 10 % (v/v) of ethanol is present in the compositions therein.

Fahim does not expressly teach that the composition is packaged in a sterile, pyrogen free form.

Wider teaches antimicrobial compositions for eliminating infections from various surfaces and materials, including the surface of the body. It is also taught that the antimicrobial compositions can be administered as a liquid either orally or through a suitable delivery system, such as a catheter. See column 1, lines 8-20; column 2, lines 30-34; and column 4, lines 10-14. It is further taught that the antimicrobial compositions are packaged in a sterile and pyrogen free form, and can be introduced into the abdominal cavity through a catheter. See column 6, lines 9-10; column 7, lines 51-55.

It would have been obvious to a person of ordinary skill in the art to employ the antimicrobial composition of Fahim in a sterile pyrogen free condition because Wider teaches antimicrobial compositions as packaged in a sterile and pyrogen free form.

One of ordinary skill in the art at the time of invention would have been motivated to employ the claimed antiseptic compositions in a sterile pyrogen free form as

conventional with antimicrobial compositions with the expectation of using the composition in catheters.

While the references does not explicitly state that "the EDTA salt provides at least 50 % of a total antimicrobial activity of the composition" as in claims 58, since Fahim discloses the same sodium salts of EDTA as that recited in the instant invention, the composition should possess claimed properties. A compound and its properties are inseparable (*IN re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963), thus, since Fahim discloses the same salts of EDTA as that recited in the instant invention, the composition should possess claimed properties.

In claims 56, 62 the intended use of a product or composition "wherein the lock flush composition is biocompatible in a patient's bloodstream", do not further limit the claim because the recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fahim (WO 00/13656), in view of Wider (US 6,500,861 B1), as applied to Claims 34, 39, 45, 56, 58, 62 above, and further in view of Root et al. (Antimicrobial Agents and Chemotherapy. Nov. 1988, pages 1627-1631, PTO-892).

Fahim, and Wider are as discussed above.

Fahim does not specifically teach the antimicrobial composition in a single-dosage vial.

Root et al. teaches a method for disinfecting a catheter by contacting (flushing) with an antimicrobial composition of aqueous EDTA solution having a concentration of 20 mg/ml. The EDTA used by Root et al. is in the form of the disodium salt. Root also teaches that the EDTA is used as a topical antiseptic in gram-negative infections. See page 1627, paragraphs 3, and 6. Root further teaches a sterile polystyrene test tubes (vials) containing the antimicrobial composition of disodium EDTA at a concentration of 20 mg/ml (2 %). See page 1628, lines 18-21.

It would have been obvious to a person of ordinary skill in the art to employ the antimicrobial composition of Fahim in a sterile condition in a single-dosage vial from the teachings of Root et al.

Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fahim (WO 00/13656, PTO-892), in view of Wilder (US 6,500,861, PTO-892), as applied to Claims 34, 39, 45, 56, 58, 62 above, and further in view Remington's Pharmaceutical Sciences.

Fahim fails to recite the employment of the composition in a prefilled syringe.

Remington's Pharmaceutical Sciences teaches sterile, pyrogen free solutions of sodium chloride as ideal for injection. It also discloses that hypodermic syringes are used for injection of liquids. See page 1837. Remington also warns against injection of

solutions containing pyrogens (See page 835, column 2, paragraph 1), and to maintain conventional sterile methodology for injected medicaments.

Possessing this teaching by Remington Pharmaceutical Sciences the skilled artisan would have been motivated to provide a syringe filled with an EDTA solution with the expectation of using such sterile, pyrogen free solution for injection.

Response to Arguments

Applicant's arguments have been considered, but not found persuasive as discussed in the previous office actions and those found below..

Applicant argues that "The sample tested in Fahim had a pH of about 7.5. In contrast, the claimed the lock flush composition has a pH of at least 9.5. The results of a dermal irritation test and an ocular irritation test with sample with a pH of 7.5 are not comparable to the results that would be obtained with a sample with a pH of 9.5. As pH is based on a logarithmic scale, there is a 100-fold difference in a pH of 7.5 compared to a pH of 9.5. Accordingly, it cannot be stated that Fahim teaches or suggest that a handwash at a pH of 9.5 is biocompatible with the epidermis and eye." These arguments have been considered, but not found persuasive because Fahim teaches that the compositions therein are safe. Fahim provides examples wherein the composition comprises 3 % by weight of tetra sodium EDTA, NaCl, water and a pH of 9.5. Fahim teaches that the pH of the compositions therein is in the range of 7.5 to 9.5. See claim 30. Fahim teaches that the composition therein are useful in cleaning skin, and the compositions are safe. See page 5, wherein it is taught that the composition therein is mild and does not irritate skin. Further, applicant merely presents statements,

conclusion or speculations or opinions regarding the pH i.e " dermal irritation test and an ocular irritation test with sample with a pH of 7.5 are not comparable to the results that would be obtained with a sample with a pH of 9.5", but fails to set forth any factual evidences.

Applicant argues that "Even if the handwash of Fahim is considered biocompatible with the epidermis and eye, this does not mean that Fahim is biocompatible in a patient's bloodstream." These arguments have been considered, but not found persuasive. It is pointed out that applicant defines bicompatibility as "the condition of being compatible with living tissue or living system by not being toxic or injurous". Fahim teaches that the skin care treatments compositions therein are safe and not toxic and biocompatable. Thus, the compositions of Fahim are biocompatible, and meet the definition of biocompatible according to applicant, since the compositions of Fahim are not toxic and did not have any adverse pharmacological effects when living tissue such as skin was exposed to the composition.

Applicant's arguments that "With an awareness of this key distinction between the effect of external (skin and eye)contact of a toxin compared to internal contact of a toxin, Dr. Olmstead and Mr. Ketteridge declared that "Fahim teaches compositions comprised of potentially toxic chemicals unsuitable for oral ingestion or parenteral administration." These remarks have been considered but not found persuasive, as discussed above the compositions of Fahim are biocompatible and meet the definition of biocompatibility.

Applicant's remarks that "Moreover, regarding the individual components of the Fahim handwash -- triclosan, PCMX, and glutaraldehyde --the Office must recognize that each is not biocompatible when given direct access into the body, when internally entering a user orally and/or parenterally to directly come into contact with the bloodstream and internal tissues." These arguments have been considered, but not found persuasive because administering a compound orally and/or parenterally is not the same as biocompatability for use in in-dwelling catheters. Toxicity of any compound depends on the amount of the compound. The amount of compounds exposed internally when used in in-dwelling catheters is very small/minor amount, and will not have any toxicity effects. Further, contrary to applicant's remarks regarding for example triclosan, it is pointed out that triclosan is a well known antimicrobial agent used in variety of products including for example toothpaste.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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